REMARKS/ARGUMENTS

Claims 1-3, 5-8 and 10-18 are currently pending in the above-identified application. Claims 1, 6, and 10 - 13 have been amended as set forth in detail below. Support for these amendments is identified in the following remarks. No new matter is added by these amendments. Claims 3, 5, 17 and 18 have been cancelled without prejudice to continued prosecution of the subject encompassed by the claims in a related co-pending application.

Rejections under 35 U.S.C. §112

Claim 1 and dependent claims 2, 3, 5, and 10-17 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner questions whether in the following recitation in claim 1 the fragment also comprises a phosphotyrosine binding domain and whether that domain can associate with the SH2 domain of Src, Abl or Fyn.

"... mammalian Dabl (Disabled protein 1) as depicted in SEQ ID NO: 3, or a fragment thereof, wherein the mammalian Disabled protein comprises a phosphotyrosine binding domain and can associate with the SH2 domain of Src, Abl or Fyn, or a complementary sequence thereof".

Applicants do not agree with the Examiner's basis for rejection, but in order to further expedite prosecution of certain subject matter disclosed and claimed in the application claims 1, and 10 have been amended. In particular, claims 1, 6, 10, and 13 have been amended to delete the phrase relating to the presence of a phosphotyrosine binding domain that can associate with the SH2 domain of Src, Abl or Fyn in the nucleotide sequence encoding the murine mouse Dab1 protein of the present invention. Further, the term "and fragment thereof" has also been deleted from claims 1, 10, and 13. The term "or a complement thereof" has been included in claims 1, 6, 10 and 13 for consistency. Therefore, independent claims 1, 6, 10 and 13

now recite a sequence encoding a murine Disabled protein 1 as depicted in SEQ. ID. NO: 3, or a complement thereof. The above amendments are believed to moot the Examiner's rejection.

Furthermore, the Examiner does not believe that claim 5 as amended further limits any nucleic acid within the scope of claim 1 will hybridize as recited in claim 5. Although Applicants do not agree with the analysis of the Examiner and in order to further expedite prosecution of certain subject matter claimed, claim 5 has been cancelled without prejudice to pursuing the prosecution of the subject matter encompassed by claim 5 in a copending related application.

Claims 11 and 12 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner has rejected these claims for the recitation "substantially depicted". The Examiner does believes that the metes and bounds of the term "substantially depicted" is unclear and has required clarification.

Although Applicants do not believe that claims 11 or 12 are indefinite for use of the term "substantially depicted" and do not acquiesce to the rejection or any remark of the Examiner, claims 11 and 12 have been amended to delete the term "substantially". This amendment is not believed to limit the claim in any way and that one of skill in the art would construe to claim in the same way if the term "substantially" were retained.

Applicants believe that each of the rejections of the Examiner under 35 U.S.C. § 112 have been addressed and overcome. Therefore, the Examiner is respectfully requested to reconsider and withdraw the rejections of claims 1, 2, 3, 5, and 10 - 17 in light of the above amends and remarks.

Rejections under 35 U.S.C. §102

Claims 1- 3, 5 stand rejected under 35 U.S.C. 102(a) as being anticipated by Howell *et. al.* (Genbank accession Y08379). Further, claims 1-3, 5-8, 10-18 (as they apply to

previous claims 1-17) stand rejected based on Howell *et al.*, *EMBO J.* 16: 121-132, 1997 (referred to herein as the Howell *et al.* reference). The Examiner has maintained this rejection because to date Applicants have not provided a declaration under 37 C.F.R. § 1.132 regarding inventorship.

Applicants provide attached hereto the Declaration of Jonathan A. Cooper. Jonathan A. Cooper is an inventor of the instant invention and a co-author of the Howell *et al.* reference and GenBank accession number Y08379. As stated in the Declaration the "Howell *et al.* reference lists as co-authors Brian W. Howell, Frank B. Gertler and Jonathan A. Cooper. (See paragraph 3). Further, GenBank Accession No. Y08379 cites the Howell *et al.* reference and indicates that the sequence was a direct submission of Brian W. Howell an inventor of the claims pending in the subject application. As set forth in paragraph 5 of the Declaration Frank B. Gertler was a post-doctoral fellow who collaborated with co-inventor Brian W. Howell on the studies to localize mDab1 expression in whole mount murine embryos as described in the Howell *et al.* reference at page 130, right column, lines 31-45 and at page 125, left column, lines 35-57. The study was conducted under the direction of Dr. Howell. As such Frank B. Gertler is not an inventor of the claims of the subject application and the Howell *et al.* reference and GenBank Accession No. Y08379 are not proper references under 35 U.S.C. § 102(a).

Applicants respectfully request the Examiner to reconsider and withdraw the present rejection of claims 1-3, and 5 under 35 U.S.C. § 102(a) as being anticipated by Howell *et al.* (GenBank Accession No. Y08379) and claims 1-3, 5-8, and 10-18 as being anticipated by Howell *et al.*, *EMBO J* 16:121-132, 1997 in view of the Declaration of Jonathan A. Cooper and the remarks above.

Rejections under 35 U.S.C. §101

Claims 1-3, 5, 6-8, 10-18 stand rejected under 35 U.S.C. §101 because the Examiner believes that the claimed invention lacks patentable utility. The Examiner has summarized claim 1 and dependent claims thereof as being drawn to a polynucleotide encoding

the polypeptide of SEQ ID NO: 3 and fragment thereof. Further, the Examiner has summarized the specification as indicating the identification of the mDab polypeptide based on its interaction with Src in a yeast two hybrid screen, disclosing that the mDab 1 mRNA is expressed as a variety of spliced mRNAs in the nervous system as in some cell lines and mDabl proteins are differentially expressed and tyrosine phosphorylated during neuronal development. Still further, the Examiner states that Applicants further assert that a complex is formed with cellular phosphotyrosyl proteins through a PTB binding domain. Finally, the Examiner believes that applicants speculate that mDab appears to playa role as an adaptor protein that participates in development of the nervous system and that applicants disclose that the PTB of mDabl interacts with a region of the amyloid precursor protein (APP) characteristic to Alzheimer's disease. Based on these findings the Examiner believes that applicants assert the utility of the invention in the diagnosis and treatment of injury and disease conditions as diverse as metastatic cancer, reactive gliosis, neurodegenerative diseases and Alzheimer's Disease.

However, the Examiner does not believe that these alleged assertions of utility are specific and substantial as the Examiner does not believe there to be substantiation that the association of mDab1 binding or the association of it's PTB domain with the diseases mentioned above such that a skilled artisan would know how to use the claimed polynucleotides to diagnose or treat any of the recited diseases. Therefore, the Examiner believes that although applicants have taken an approach and direction that potentially may lead to elucidating the specific function of mDab1 gene and the fragments thereof, the claimed invention is incomplete and does not have a patentable utility until some actual and specific disease condition can be associated with the ability of mDab 1 (SEQ ID NO: 3) to bind to the SH2 domain of Abl, Fyn and or Src and/or it's PTB domain.

When making a rejection under 35 U.S.C. § 101 for lack of utility the initial burden is on the Office to establish a *prima facie* case and to provide evidentiary support. (MPEP § 2107.02(IV)). In particular, where the asserted utility is not believed to be specific or substantial, a *prima facie* show must establish that it is more likely than not that a person of

ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial and the showing must contain i) an explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is neither both specific and substantial nor well-established; ii) support for factual findings relied upon in reaching this conclusion; and iii) an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. Applicants do not believe that the Examiner has met the burden for establishing a *prima facie* case for lack of utility. In particular, Applicants do not believe that the Examiner has properly summarized all of the utilities set forth in the specification as filed, nor has the Examiner provided an evaluation of all relevant evidence of record, including utilities taught in the closest prior art.

Further, Applicants have set forth a number of utilities for the present claimed invention in the specification as filed. In particular, the Examiner is invited to review for example, page 4, lines 25 - 28, page 17, line 23, page 18, lines 5-10 and page 20, lines 21-33, wherein Applicants provide that the invention demonstrates that disruption of mDab1 gene disturbs neuronal layering in cerebral cortex, hippocampus and cerebellum. It was well known prior to the present invention that such neuronal developmental disruptions were associated with, for example, behavioral defects such as ataxia, tremors, imbalance and a reeling gait as exemplified by the mice with the reelin mutation. Therefore, as stated in the specification at page 20, lines 21-33 "the polynucleotides molecules, proteins, peptides and antibodies of the present invention are useful in *in vitro* assays to screen for compounds capable of modulating the activity or expression of mDab1. Within these methods, the *mdab1* gene and mDab1 proteins and peptides disclosed herein are useful for generating, isolating, and characterizing endogenous and exogenous factors, drugs, and other agents that can be employed in methods to evaluate and/or regulate processes involved in normal and abnormal cell migration." (emphasis added). Additional uses of the polynucleotide, protein and peptide molecules of the present invention are also disclosed in the specification as filed.

Applicants also note:

> Rejections under 35 U.S.C. 101 have been rarely sustained by federal courts. Generally speaking, in these rare cases, the 35 U.S.C. 101 rejection was sustained either because the applicant failed to disclose any utility for the invention or asserted a utility that could only be true if it violated a scientific principle, such as the second law of thermodynamics, or a law of nature, or was wholly inconsistent with contemporary knowledge in the art. *In re Gazave*, 379 F.2d 973, 978, 154 USPQ 92, 96 (CCPA 1967). Special care therefore should be taken when assessing the credibility of an asserted therapeutic utility for a claimed invention.

MPEP § 2107.02 (III)(B) (emphasis original).

In the present case, Applicants have provided a number of uses for the molecules of the present invention and there is no reasonable basis for maintaining that Applicants' asserted utility violates a scientific principle or a law of nature, or is wholly inconsistent with contemporary knowledge in the art. To the contrary, the totality of the evidence of record not only shows that Applicants' asserted utility is believable to a person of ordinary skill in the art, but is in fact operable according to the teachings provided in the specification. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 101.

Rejections under 35 U.S.C. §112

Claims 1, 2, 5, 6-8, 11-12 stand newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner believes that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. In particular the Examiner does not believe that the specification contains any disclosure of the structure of all DNA sequences of all mammalian mDab1 and fragments thereof. Further, the Examiner believes that the genus of polynucleotides that encode polypeptides that comprise any mammalian Dab1 or any fragment thereof, is a large variable genus with the potentiality of encoding many different proteins from any mammalian source and therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences and sequences that have not been disclosed by the specification. Also, because the specification discloses only a few (three) species of the claimed genus the Examiner believes that the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus including any polynucleotide encoding any polypeptide with the sole limitation of having a phosphotyrosine binding domain and being capable of associating with Src, Abl or Fyn as there are other genes encoding polypeptides. Therefore, the Examiner does not believe that one skilled in the art can reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Although Applicants believe that the full scope of the invention as claimed is fully described and enabled as required under 35 U.S.C. § 112, first paragraph, and in order to further expedite prosecution of certain subject matter disclosed and claimed in the instant application, claims 1, 6, 10 and 13 have been amended to delete the phrase "fragments thereof." Further, claim 5 has been cancelled without prejudice. Applicants believe that the rejections of claims 1, 2, 6-8, 11-12 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description and enablement requirements are moot.

Further, claims 1, 2, 5-8, 11 and 12 stand newly rejected under 35 U.S.C. 112, first paragraph, because the Examiner believes that the specification, while being enabling for a DNA sequence of SEQ ID NO: 3, does not reasonably provide enablement for any fragment thereof. The Examiner does not believe that the specification enables any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention

commensurate in scope with these claims. Further, the Examiner does not believe that the specification supports the broad scope of the claims which encompass any polynucleotide that will hybridize to SEQ ID NO: 2, any ortholog, allelic or splice variant of the polypeptide of SEQ ID NO: 3 encoded by SEQ ID NO: 2, as well as any polynucleotide comprising 15-60 nucleotides that can hybridize to SEQ ID NO: 2 because the specification does not establish: (A) regions of the polynucleotide sequence which may be modified without necessarily affecting the protein structure necessary for it's ability to specifically associate with Src, Abl or Fyn or conserve the PTB domain; (B) the general tolerance of the polynucleotide encoding the specific mDab1 to modification and extent of such tolerance; (C) a rational and predictable scheme for selecting a fragment of a polynucleotide sequence with an expectation of retaining the ability to hybridize to a polynucleotide sequence encoding mDab 1 encoded by SEQ ID NO: 2 (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Although Applicants believe that the full scope of the invention as recited in claims 1, 2, 5-8, 11 and 12 is fully enabled under 35 U.S.C. § 112, first paragraph, and in order to further expedite prosecution of certain subject matter disclosed and claimed in the instant application, claim 6 has been amended to delete the phrase "allelic and species variants thereof, wherein the mammalian Disabled protein, allelic pr species variant thereof comprises a phosphotyrosine binding domain and can associate with the SH2 domain of Src, Abl or Fyn." Also, claims 3, 17 and 18 have been cancelled because the subject matter of the claims has been incorporated into claims 1, and 13 respectively. Further, claim 5 has been cancelled without prejudice. Applicants believe that the rejections of claims 1, 2, 6-8, 11 and 12 under 35 U.S.C. 112, first paragraph, as failing to fully enable the full scope of the invention is moot and reconsideration of the pending claims is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: 28 June 2006 By: _____

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